



## SEQUENCE LISTING

14/C  
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MAY 28 2002  
TECH CENTER 1600/2900

SubD1  
<110> Krohn, Kai  
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<120> NOVEL GENE DEFECTIVE IN APECED AND ITS USE

<130> U0126539

<140> 09/508,658

<141> 2000-11-03

<150> PCT/FI98/00749

<151> 1998-09-23

<150> 973762

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<170> PatentIn Ver. 2.0

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| Glu Asp Ser Gly Ser Gly Lys Asn Lys Ala Arg Ser Ser Ser Gly Pro |      |
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| gcc cgc ctg gcc cct ggg cct gcc aag gat gac act gcc agt cac gag   | 1660 |
| Ala Arg Leu Ala Pro Gly Pro Ala Lys Asp Asp Thr Ala Ser His Glu   |      |
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| ccc gct ctg cac agg gat gac ctg gag tcc ctt ctg agc gag cac acc   | 1708 |
| Pro Ala Leu His Arg Asp Asp Leu Glu Ser Leu Leu Ser Glu His Thr   |      |
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| Glu | Ile | Ala | Val | Ala | Val | Asp | Ser | Ala | Phe | Pro | Leu | Leu | His | Ala | Leu |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Ala | Asp | His | Asp | Val | Val | Pro | Glu | Asp | Lys | Phe | Gln | Glu | Thr | Leu | His |
|     |     | 35  |     |     |     |     |     | 40  |     |     |     | 45  |     |     |     |
| Leu | Lys | Glu | Lys | Glu | Gly | Cys | Pro | Gln | Ala | Phe | His | Ala | Leu | Leu | Ser |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Trp | Leu | Leu | Thr | Gln | Asp | Ser | Thr | Ala | Ile | Leu | Asp | Phe | Trp | Arg | Val |
| 65  |     |     |     | 70  |     |     |     |     |     | 75  |     |     |     |     | 80  |
| Leu | Phe | Lys | Asp | Tyr | Asn | Leu | Glu | Arg | Tyr | Gly | Arg | Leu | Gln | Pro | Ile |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Leu | Asp | Ser | Phe | Pro | Lys | Asp | Val | Asp | Leu | Ser | Gln | Pro | Arg | Lys | Gly |
|     |     | 100 |     |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Arg | Lys | Pro | Pro | Ala | Val | Pro | Lys | Ala | Leu | Val | Pro | Pro | Pro | Arg | Leu |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Pro | Thr | Lys | Arg | Lys | Ala | Ser | Glu | Glu | Ala | Arg | Ala | Ala | Ala | Pro | Ala |
|     | 130 |     |     |     |     | 135 |     |     |     | 140 |     |     |     |     |     |
| Ala | Leu | Thr | Pro | Arg | Gly | Thr | Ala | Ser | Pro | Gly | Ser | Gln | Leu | Lys | Ala |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Lys | Pro | Pro | Lys | Lys | Pro | Glu | Ser | Ser | Ala | Glu | Gln | Gln | Arg | Leu | Pro |
|     |     |     | 165 |     |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Leu | Gly | Asn | Gly | Ile | Gln | Thr | Met | Ser | Ala | Ser | Val | Gln | Arg | Ala | Val |
|     |     | 180 |     |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| Ala | Met | Ser | Ser | Gly | Asp | Val | Pro | Gly | Ala | Arg | Gly | Ala | Val | Glu | Gly |

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|---|-----|---------|
| 195   | 200 | 205     |
| Ile Leu Ile Gln Gln Val Phe Glu Ser Gly Gly Ser Lys Lys Cys Ile |     |         |
| 210   | 215 | 220     |
| Gln Val Gly Gly Glu Phe Tyr Thr Pro Ser Lys Phe Glu Asp Ser Gly |     |         |
| 225   | 230 | 235 240 |
| Ser Gly Lys Asn Lys Ala Arg Ser Ser Ser Gly Pro Lys Pro Leu Val |     |         |
|   | 245 | 250 255 |
| Arg Ala Lys Gly Ala Gln Gly Ala Ala Pro Gly Gly Gly Glu Ala Arg |     |         |
|   | 260 | 265 270 |
| Leu Gly Gln Gln Gly Ser Val Pro Ala Pro Leu Ala Leu Pro Ser Asp |     |         |
|   | 275 | 280 285 |
| Pro Gln Leu His Gln Lys Asn Glu Asp Glu Cys Ala Val Cys Arg Asp |     |         |
|   | 290 | 295 300 |
| Gly Gly Glu Leu Ile Cys Cys Asp Gly Cys Pro Arg Ala Phe His Leu |     |         |
| 305   | 310 | 315 320 |
| Ala Cys Leu Ser Pro Pro Leu Arg Glu Ile Pro Ser Gly Thr Trp Arg |     |         |
|   | 325 | 330 335 |
| Cys Ser Ser Cys Leu Gln Ala Thr Val Gln Glu Val Gln Pro Arg Ala |     |         |
|   | 340 | 345 350 |
| Glu Glu Pro Arg Pro Gln Glu Pro Pro Val Glu Thr Pro Leu Pro Pro |     |         |
|   | 355 | 360 365 |
| Gly Leu Arg Ser Ala Gly Glu Glu Val Arg Gly Pro Pro Gly Glu Pro |     |         |
|   | 370 | 375 380 |
| Leu Ala Gly Met Asp Thr Thr Leu Val Tyr Lys His Leu Pro Ala Pro |     |         |
| 385   | 390 | 395 400 |
| Pro Ser Ala Ala Pro Leu Pro Gly Leu Asp Ser Ser Ala Leu His Pro |     |         |
|   | 405 | 410 415 |
| Leu Leu Cys Val Ala Pro Glu Gly Gln Gln Asn Leu Ala Pro Gly Ala |     |         |
|   | 420 | 425 430 |
| Arg Cys Gly Val Cys Gly Asp Gly Thr Asp Val Leu Arg Cys Thr His |     |         |
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| Cys Ala Ala Ala Phe His Trp Arg Cys His Phe Pro Ala Gly Thr Ser |     |         |



|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Trp | Leu | Val | Tyr | Ser | Ser | Gly | Ala | Pro | Gly | Thr | Gln | Gln | Pro | Ala | Arg |     |  |
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| aac | cgg | gtt | ttc | ttc | cca | ata | ggg | atg | gcc | ccg | ggg | ggg | gtc | tgt | tcg | 335 |  |
| Asn | Arg | Val | Phe | Phe | Pro | Ile | Gly | Met | Ala | Pro | Gly | Gly | Val | Cys | Ser |     |  |
|     |     | 20  |     |     |     |     | 25  |     |     |     | 30  |     |     |     |     |     |  |
| aga | cca | gat | gga | tgg | gga | aca | ggg | ggg | cag | ggc | aga | att | tca | ggc | cct | 383 |  |
| Arg | Pro | Asp | Gly | Trp | Gly | Thr | Gly | Gly | Gln | Gly | Arg | Ile | Ser | Gly | Pro |     |  |
|     |     | 35  |     |     |     | 40  |     |     |     |     | 45  |     |     |     |     |     |  |
| ggc | agc | atg | gga | gca | ggg | cag | aga | ctg | ggg | agt | tca | ggg | acc | cag | aga | 431 |  |
| Gly | Ser | Met | Gly | Ala | Gly | Gln | Arg | Leu | Gly | Ser | Ser | Gly | Thr | Gln | Arg |     |  |
|     | 50  |     |     |     | 55  |     |     |     | 60  |     |     |     |     |     | 65  |     |  |
| tgc | tgc | tgg | ggg | agc | tgt | ttt | ggg | aag | gag | gtg | gct | ctc | agg | agg | gtg | 479 |  |
| Cys | Cys | Trp | Gly | Ser | Cys | Phe | Gly | Lys | Glu | Val | Ala | Leu | Arg | Arg | Val |     |  |
|     |     |     |     | 70  |     |     |     | 75  |     |     |     |     |     | 80  |     |     |  |
| ctg | cac | ccc | agc | cca | gtc | tgc | atg | ggc | gtc | tct | tgc | ctg | tgc | cag | aag | 527 |  |
| Leu | His | Pro | Ser | Pro | Val | Cys | Met | Gly | Val | Ser | Cys | Leu | Cys | Gln | Lys |     |  |
|     |     |     | 85  |     |     |     |     | 90  |     |     |     |     |     | 95  |     |     |  |
| aat | gag | gac | gag | tgt | gcc | gtg | tgt | cgg | gac | ggc | ggg | gag | ctc | atc | tgc | 575 |  |
| Asn | Glu | Asp | Glu | Cys | Ala | Val | Cys | Arg | Asp | Gly | Gly | Glu | Leu | Ile | Cys |     |  |
|     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |     |  |
| tgt | gac | ggc | tgc | cct | cgg | gcc | ttc | cac | ctg | gcc | tgc | ctg | tcc | cct | cgg | 623 |  |
| Cys | Asp | Gly | Cys | Pro | Arg | Ala | Phe | His | Leu | Ala | Cys | Leu | Ser | Pro | Pro |     |  |
|     |     | 115 |     |     |     | 120 |     |     |     |     | 125 |     |     |     |     |     |  |
| ctc | cgg | gag | atc | ccc | agt | ggg | acc | tgg | agg | tgc | tcc | agc | tgc | ctg | cag | 671 |  |
| Leu | Arg | Glu | Ile | Pro | Ser | Gly | Thr | Trp | Arg | Cys | Ser | Ser | Cys | Leu | Gln |     |  |
|     |     | 130 |     |     |     | 135 |     |     |     | 140 |     |     |     |     | 145 |     |  |
| gca | aca | gtc | cag | gag | gtg | cag | ccc | cgg | gca | gag | gag | ccc | cgg | ccc | cag | 719 |  |
| Ala | Thr | Val | Gln | Glu | Val | Gln | Pro | Arg | Ala | Glu | Glu | Pro | Arg | Pro | Gln |     |  |
|     |     |     | 150 |     |     |     |     |     | 155 |     |     |     |     | 160 |     |     |  |
| gag | cca | ccc | gtg | gag | acc | ccg | ctc | ccc | ccg | ggg | ctt | agg | tcg | gcg | gga | 767 |  |
| Glu | Pro | Pro | Val | Glu | Thr | Pro | Leu | Pro | Pro | Gly | Leu | Arg | Ser | Ala | Gly |     |  |
|     |     |     | 165 |     |     |     | 170 |     |     |     |     |     | 175 |     |     |     |  |
| gag | gag | gta | aga | ggg | cca | cct | ggg | gaa | ccc | cta | gcc | ggc | atg | gac | acg | 815 |  |
| Glu | Glu | Val | Arg | Gly | Pro | Pro | Gly | Glu | Pro | Leu | Ala | Gly | Met | Asp | Thr |     |  |
|     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |     |     |  |
| act | ctt | gtc | tac | aag | cac | ctg | ccg | gct | ccg | cct | tct | gca | gcc | ccg | ctg | 863 |  |



|            |            |            |            |              |             |     |     |     |     |     |     |            |     |     |     |      |      |
|------------|------------|------------|------------|--------------|-------------|-----|-----|-----|-----|-----|-----|------------|-----|-----|-----|------|------|
| Thr        | Leu        | Val        | Tyr        | Lys          | His         | Leu | Pro | Ala | Pro | Pro | Ser | Ala        | Ala | Pro | Leu |      |      |
| 195        |            |            |            |              |             | 200 |     |     |     |     | 205 |            |     |     |     |      |      |
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| Pro        | Gly        | Leu        | Asp        | Ser          | Ser         | Ala | Leu | His | Pro | Leu | Leu | Cys        | Val | Gly | Pro |      |      |
| 210        |            |            |            | 215          |             |     |     |     | 220 |     |     |            |     | 225 |     |      |      |
| gag        | ggt        | cag        | cag        | aac          | ctg         | gct | cct | ggt | gcg | cgt | tgc | ggg        | gtg | tgc | gga | 959  |      |
| Glu        | Gly        | Gln        | Gln        | Asn          | Leu         | Ala | Pro | Gly | Ala | Arg | Cys | Gly        | Val | Cys | Gly |      |      |
|            |            |            |            | 230          |             |     |     |     | 235 |     |     |            |     | 240 |     |      |      |
| gat        | ggt        | acg        | gac        | gtg          | ctg         | cgg | tgt | act | cac | tgc | gcc | gct        | gcc | ttc | cac | 1007 |      |
| Asp        | Gly        | Thr        | Asp        | Val          | Leu         | Arg | Cys | Thr | His | Cys | Ala | Ala        | Ala | Phe | His |      |      |
|            |            |            | 245        |              |             |     |     | 250 |     |     |     |            |     | 255 |     |      |      |
| tgg        | cgc        | tgc        | cac        | ttc          | cca         | gcc | ggc | acc | tcc | cgg | ccc | ggg        | acg | ggc | ctg | 1055 |      |
| Trp        | Arg        | Cys        | His        | Phe          | Pro         | Ala | Gly | Thr | Ser | Arg | Pro | Gly        | Thr | Gly | Leu |      |      |
|            |            | 260        |            |              |             |     | 265 |     |     |     |     | 270        |     |     |     |      |      |
| cgc        | tgc        | aga        | tcc        | tgc          | tca         | gga | gac | gtg | acc | cca | gcc | cct        | gtg | gag | ggg | 1103 |      |
| Arg        | Cys        | Arg        | Ser        | Cys          | Ser         | Gly | Asp | Val | Thr | Pro | Ala | Pro        | Val | Glu | Gly |      |      |
|            | 275        |            |            |              |             | 280 |     |     |     |     | 285 |            |     |     |     |      |      |
| gtg        | ctg        | gcc        | ccc        | agc          | ccc         | gcc | cgc | ctg | gcc | cct | ggg | cct        | gcc | aag | gat | 1151 |      |
| Val        | Leu        | Ala        | Pro        | Ser          | Pro         | Ala | Arg | Leu | Ala | Pro | Gly | Pro        | Ala | Lys | Asp |      |      |
| 290        |            |            |            |              | 295         |     |     |     |     | 300 |     |            |     |     | 305 |      |      |
| gac        | act        | gcc        | agt        | cac          | gag         | ccc | gct | ctg | cac | agg | gat | gac        | ctg | gag | tcc | 1199 |      |
| Asp        | Thr        | Ala        | Ser        | His          | Glu         | Pro | Ala | Leu | His | Arg | Asp | Asp        | Leu | Glu | Ser |      |      |
|            |            |            |            | 310          |             |     |     |     | 315 |     |     |            |     | 320 |     |      |      |
| ctt        | ctg        | agc        | gag        | cac          | acc         | ttc | gat | ggc | atc | ctg | cag | tgg        | gcc | atc | cag | 1247 |      |
| Leu        | Leu        | Ser        | Glu        | His          | Thr         | Phe | Asp | Gly | Ile | Leu | Gln | Trp        | Ala | Ile | Gln |      |      |
|            |            |            | 325        |              |             |     |     | 330 |     |     |     |            | 335 |     |     |      |      |
| agc        | atg        | gcc        | cgt        | ccg          | gcg         | gcc | ccc | ttc | ccc | tcc | tga | ccccagatgg |     |     |     | 1293 |      |
| Ser        | Met        | Ala        | Arg        | Pro          | Ala         | Ala | Pro | Phe | Pro | Ser |     |            |     |     |     |      |      |
|            |            | 340        |            |              |             | 345 |     |     |     |     |     |            |     |     |     |      |      |
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| aagccggccg | gctgggatca | agaaggggac | agcgccacct | cttg tca gtc | ctcg gctgta |     |     |     |     |     |     |            |     |     |     | 1413 |      |
| aacagctctg | tgtttctggg | gacaccagcc | atcatgtgcc | tg gaaattaa  | accctgcccc  |     |     |     |     |     |     |            |     |     |     | 1473 |      |
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| Met | Trp | Leu | Val | Tyr | Ser | Ser | Gly | Ala | Pro | Gly | Thr | Gln | Gln | Pro | Ala |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Arg | Asn | Arg | Val | Phe | Phe | Pro | Ile | Gly | Met | Ala | Pro | Gly | Gly | Val | Cys |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Ser | Arg | Pro | Asp | Gly | Trp | Gly | Thr | Gly | Gly | Gln | Gly | Arg | Ile | Ser | Gly |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Pro | Gly | Ser | Met | Gly | Ala | Gly | Gln | Arg | Leu | Gly | Ser | Ser | Gly | Thr | Gln |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Arg | Cys | Cys | Trp | Gly | Ser | Cys | Phe | Gly | Lys | Glu | Val | Ala | Leu | Arg | Arg |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Val | Leu | His | Pro | Ser | Pro | Val | Cys | Met | Gly | Val | Ser | Cys | Leu | Cys | Gln |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Lys | Asn | Glu | Asp | Glu | Cys | Ala | Val | Cys | Arg | Asp | Gly | Gly | Glu | Leu | Ile |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Cys | Cys | Asp | Gly | Cys | Pro | Arg | Ala | Phe | His | Leu | Ala | Cys | Leu | Ser | Pro |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Pro | Leu | Arg | Glu | Ile | Pro | Ser | Gly | Thr | Trp | Arg | Cys | Ser | Ser | Cys | Leu |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Gln | Ala | Thr | Val | Gln | Glu | Val | Gln | Pro | Arg | Ala | Glu | Glu | Pro | Arg | Pro |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Gln | Glu | Pro | Pro | Val | Glu | Thr | Pro | Leu | Pro | Pro | Gly | Leu | Arg | Ser | Ala |
|     |     |     |     | 165 |     |     |     | 170 |     |     |     |     |     | 175 |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Gly | Glu | Glu | Val | Arg | Gly | Pro | Pro | Gly | Glu | Pro | Leu | Ala | Gly | Met | Asp |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Thr | Thr | Leu | Val | Tyr | Lys | His | Leu | Pro | Ala | Pro | Pro | Ser | Ala | Ala | Pro |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| Leu | Pro | Gly | Leu | Asp | Ser | Ser | Ala | Leu | His | Pro | Leu | Leu | Cys | Val | Gly |

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|---|-----|---------|
| 210   | 215 | 220     |
| Pro Glu Gly Gln Gln Asn Leu Ala Pro Gly Ala Arg Cys Gly Val Cys |     |         |
| 225   | 230 | 235 240 |
| Gly Asp Gly Thr Asp Val Leu Arg Cys Thr His Cys Ala Ala Ala Phe |     |         |
|   | 245 | 250 255 |
| His Trp Arg Cys His Phe Pro Ala Gly Thr Ser Arg Pro Gly Thr Gly |     |         |
|   | 260 | 265 270 |
| Leu Arg Cys Arg Ser Cys Ser Gly Asp Val Thr Pro Ala Pro Val Glu |     |         |
|   | 275 | 280 285 |
| Gly Val Leu Ala Pro Ser Pro Ala Arg Leu Ala Pro Gly Pro Ala Lys |     |         |
|   | 290 | 295 300 |
| Asp Asp Thr Ala Ser His Glu Pro Ala Leu His Arg Asp Asp Leu Glu |     |         |
| 305   | 310 | 315 320 |
| Ser Leu Leu Ser Glu His Thr Phe Asp Gly Ile Leu Gln Trp Ala Ile |     |         |
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Trp Leu Val Tyr Ser Ser Gly Ala Pro Gly Thr Gln Gln Pro Ala Arg  
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Arg Pro Asp Gly Trp Gly Thr Gly Gly Gln Gly Arg Ile Ser Gly Pro  
35 40 45

ggc agc atg gga gca ggg cag aga ctg ggg agt tca ggt acc cag aga 431  
Gly Ser Met Gly Ala Gly Gln Arg Leu Gly Ser Ser Gly Thr Gln Arg  
50 55 60 65

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Cys Cys Trp Gly Ser Cys Phe Gly Lys Glu Val Ala Leu Arg Arg Val  
70 75 80

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85 90 95

aat gag gac gag tgt gcc gtg tgt cgg gac ggc ggg gag ctc atc tgc 575  
Asn Glu Asp Glu Cys Ala Val Cys Arg Asp Gly Gly Glu Leu Ile Cys  
100 105 110

tgt gac ggc tgc cct cgg gcc ttc cac ctg gcc tgc ctg tcc cct ccg 623  
Cys Asp Gly Cys Pro Arg Ala Phe His Leu Ala Cys Leu Ser Pro Pro  
115 120 125

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Ala Thr Val Gln Glu Val Gln Pro Arg Ala Glu Glu Pro Arg Pro Gln  
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165 170 175

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 Glu Glu Pro Arg Cys Gln Gly Trp Thr Pro Arg Pro Cys Thr Pro Tyr  
 180 185 190

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 Cys Val Trp Val Leu Arg Val Ser Arg Thr Trp Leu Leu Val Arg Val  
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 Ala Gly Cys Ala Glu Met Val Arg Thr Cys Cys Gly Val Leu Thr Ala  
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 230 235 240

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| Thr | Leu | His | Leu | Lys | Glu | Lys | Glu | Gly | Cys | Pro | Val | Gln | Ala | Phe | His |
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| Cys | Lys | Asn | Lys | Ala | Arg | Ser | Ser | Ser | Gly | Pro | Lys | Pro | Leu | Val |
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<110> Krohn, Kai  
 Heino, Maarit  
 Peterson, Part  
 Scott S., Hamish  
 Antonarakis E., Stylianos  
 Lalioti D., Maria  
 Shimizu, Nobuyoshi  
 Kudoh, Jun

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Met Ala Thr Asp Ala Ala Leu Arg Arg Leu Leu Arg  
1 5 10

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Leu His Arg Thr Glu Ile Ala Val Ala Val Asp Ser Ala Phe Pro Leu  
15 20 25

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Leu His Ala Leu Ala Asp His Asp Val Val Pro Glu Asp Lys Phe Gln  
30 35 40

gag acg ctt cat ctg aag gaa aag gag ggc tgc ccc cag gcc ttc cac 316  
Glu Thr Leu His Leu Lys Glu Lys Glu Gly Cys Pro Gln Ala Phe His  
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gcc ctc ctg tcc tgg ctg ctg acc cag gac tcc aca gcc atc ctg gac 364  
Ala Leu Leu Ser Trp Leu Leu Thr Gln Asp Ser Thr Ala Ile Leu Asp  
65 70 75

ttc tgg agg gtg ctg ttc aag gac tac aac ctg gag cgc tat ggc cgg 412  
Phe Trp Arg Val Leu Phe Lys Asp Tyr Asn Leu Glu Arg Tyr Gly Arg  
80 85 90

ctg cag ccc atc ctg gac agc ttc ccc aaa gat gtg gac ctc agc cag 460  
Leu Gln Pro Ile Leu Asp Ser Phe Pro Lys Asp Val Asp Leu Ser Gln  
95 100 105

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Gln Leu Lys Ala Lys Pro Pro Lys Lys Pro Glu Ser Ser Ala Glu Gln  
160 165 170

cag cgc ctt cca ctc ggg aac ggg att cag acc atg tca gct tca gtc 700  
Gln Arg Leu Pro Leu Gly Asn Gly Ile Gln Thr Met Ser Ala Ser Val  
175 180 185



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| Gln Arg Ala Val Ala Met Ser Ser Gly Asp Val Pro Gly Ala Arg Gly |      |
| 190 195 200   |      |
| gcc gtg gag ggg atc ctc atc cag cag gtg ttt gag tca ggc ggc tcc | 796  |
| Ala Val Glu Gly Ile Leu Ile Gln Gln Val Phe Glu Ser Gly Gly Ser |      |
| 205 210 215 220   |      |
| aag aag tgc atc cag gtt ggc ggg gag ttc tac act ccc agc aag ttc | 844  |
| Lys Lys Cys Ile Gln Val Gly Gly Glu Phe Tyr Thr Pro Ser Lys Phe |      |
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| Glu Asp Ser Gly Ser Gly Lys Asn Lys Ala Arg Ser Ser Ser Gly Pro |      |
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| Lys Pro Leu Val Arg Ala Lys Gly Ala Gln Gly Ala Ala Pro Gly Gly |      |
| 255 260 265   |      |
| ggt gag gct agg ctg ggc cag cag ggc agc gtt ccc gcc cct ctg gcc | 988  |
| Gly Glu Ala Arg Leu Gly Gln Gln Gly Ser Val Pro Ala Pro Leu Ala |      |
| 270 275 280   |      |
| ctc ccc agt gac ccc cag ctc cac cag aag aat gag gac gag tgt gcc | 1036 |
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| 285 290 295 300   |      |
| gtg tgt cgg gac ggc ggg gag ctc atc tgc tgt gac ggc tgc cct cgg | 1084 |
| Val Cys Arg Asp Gly Gly Glu Leu Ile Cys Cys Asp Gly Cys Pro Arg |      |
| 305 310 315   |      |
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| Ala Phe His Leu Ala Cys Leu Ser Pro Pro Leu Arg Glu Ile Pro Ser |      |
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| ggg acc tgg agg tgc tcc agc tgc ctg cag gca aca gtc cag gag gtg | 1180 |
| Gly Thr Trp Arg Cys Ser Ser Cys Leu Gln Ala Thr Val Gln Glu Val |      |
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| 365 370 375 380   |      |

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| Pro Gly Glu Pro Leu Ala Gly Met Asp Thr Thr Leu Val Tyr Lys His    |      |
| 385 390 395  |      |
| ctg ccg gct ccg cct tct gca gcc ccg ctg cca ggg ctg gac tcc tcg    | 1372 |
| Leu Pro Ala Pro Pro Ser Ala Ala Pro Leu Pro Gly Leu Asp Ser Ser    |      |
| 400 405 410  |      |
| gcc ctg cac ccc cta ctg tgt gtg gct cct gag ggt cag cag aac ctg    | 1420 |
| Ala Leu His Pro Leu Leu Cys Val Ala Pro Glu Gly Gln Gln Asn Leu    |      |
| 415 420 425  |      |
| gct cct ggt gcg cgt tgc ggg gtg tgc gga gat ggt acg gac gtg ctg    | 1468 |
| Ala Pro Gly Ala Arg Cys Gly Val Cys Gly Asp Gly Thr Asp Val Leu    |      |
| 430 435 440  |      |
| cgg tgt act cac tgc gcc gct gcc ttc cac tgg cgc tgc cac ttc cca    | 1516 |
| Arg Cys Thr His Cys Ala Ala Ala Phe His Trp Arg Cys His Phe Pro    |      |
| 445 450 455 460  |      |
| gcc ggc acc tcc ccg ccc ggg acg ggc ctg cgc tgc aga tcc tgc tca    | 1564 |
| Ala Gly Thr Ser Arg Pro Gly Thr Gly Leu Arg Cys Arg Ser Cys Ser    |      |
| 465 470 475  |      |
| gga gac gtg acc cca gcc cct gtg gag ggg gtg ctg gcc ccc agc ccc    | 1612 |
| Gly Asp Val Thr Pro Ala Pro Val Glu Gly Val Leu Ala Pro Ser Pro    |      |
| 480 485 490  |      |
| gcc cgc ctg gcc cct ggg cct gcc aag gat gac act gcc agt cac gag    | 1660 |
| Ala Arg Leu Ala Pro Gly Pro Ala Lys Asp Asp Thr Ala Ser His Glu    |      |
| 495 500 505  |      |
| ccc gct ctg cac agg gat gac ctg gag tcc ctt ctg agc gag cac acc    | 1708 |
| Pro Ala Leu His Arg Asp Asp Leu Glu Ser Leu Ser Glu His Thr        |      |
| 510 515 520  |      |
| ttc gat ggc atc ctg cag tgg gcc atc cag agc atg gcc cgt ccg gcg    | 1756 |
| Phe Asp Gly Ile Leu Gln Trp Ala Ile Gln Ser Met Ala Arg Pro Ala    |      |
| 525 530 535 540  |      |
| gcc ccc ttc ccc tcc tga cccagatgg ccgggacatg cagctctgat            | 1804 |
| Ala Pro Phe Pro Ser  |      |
| 545  |      |
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| agaaggggac agcgccacct cttgtcagtg ctgggctgta aacagctctg tgtttctggg  | 1924 |

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ala | Thr | Asp | Ala | Ala | Leu | Arg | Arg | Leu | Leu | Arg | Leu | His | Arg | Thr |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Glu | Ile | Ala | Val | Ala | Val | Asp | Ser | Ala | Phe | Pro | Leu | Leu | His | Ala | Leu |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Asp | His | Asp | Val | Val | Pro | Glu | Asp | Lys | Phe | Gln | Glu | Thr | Leu | His |
|     |     | 35  |     |     |     |     |     | 40  |     |     |     | 45  |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Lys | Glu | Lys | Glu | Gly | Cys | Pro | Gln | Ala | Phe | His | Ala | Leu | Leu | Ser |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Trp | Leu | Leu | Thr | Gln | Asp | Ser | Thr | Ala | Ile | Leu | Asp | Phe | Trp | Arg | Val |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Phe | Lys | Asp | Tyr | Asn | Leu | Glu | Arg | Tyr | Gly | Arg | Leu | Gln | Pro | Ile |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Asp | Ser | Phe | Pro | Lys | Asp | Val | Asp | Leu | Ser | Gln | Pro | Arg | Lys | Gly |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Arg | Lys | Pro | Pro | Ala | Val | Pro | Lys | Ala | Leu | Val | Pro | Pro | Pro | Arg | Leu |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Pro | Thr | Lys | Arg | Lys | Ala | Ser | Glu | Glu | Ala | Arg | Ala | Ala | Ala | Pro | Ala |
|     | 130 |     |     |     |     | 135 |     |     |     | 140 |     |     |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Leu | Thr | Pro | Arg | Gly | Thr | Ala | Ser | Pro | Gly | Ser | Gln | Leu | Lys | Ala |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Lys | Pro | Pro | Lys | Lys | Pro | Glu | Ser | Ser | Ala | Glu | Gln | Gln | Arg | Leu | Pro |
|     |     |     | 165 |     |     |     |     |     | 170 |     |     |     |     | 175 |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Gly | Asn | Gly | Ile | Gln | Thr | Met | Ser | Ala | Ser | Val | Gln | Arg | Ala | Val |
|     |     | 180 |     |     |     |     |     | 185 |     |     |     |     | 190 |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Met | Ser | Ser | Gly | Asp | Val | Pro | Gly | Ala | Arg | Gly | Ala | Val | Glu | Gly |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|

| 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     |     |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Ile | Leu | Ile | Gln | Gln | Val | Phe | Glu | Ser | Gly | Gly | Ser | Lys | Lys | Cys | Ile |  |
| 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |     |  |
| Gln | Val | Gly | Gly | Glu | Phe | Tyr | Thr | Pro | Ser | Lys | Phe | Glu | Asp | Ser | Gly |  |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |  |
| Ser | Gly | Lys | Asn | Lys | Ala | Arg | Ser | Ser | Ser | Gly | Pro | Lys | Pro | Leu | Val |  |
| 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |     |     |     |     |  |
| Arg | Ala | Lys | Gly | Ala | Gln | Gly | Ala | Ala | Pro | Gly | Gly | Gly | Glu | Ala | Arg |  |
| 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |     |     |     |  |
| Leu | Gly | Gln | Gln | Gly | Ser | Val | Pro | Ala | Pro | Leu | Ala | Leu | Pro | Ser | Asp |  |
| 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |     |     |  |
| Pro | Gln | Leu | His | Gln | Lys | Asn | Glu | Asp | Glu | Cys | Ala | Val | Cys | Arg | Asp |  |
| 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |     |  |
| Gly | Gly | Glu | Leu | Ile | Cys | Cys | Asp | Gly | Cys | Pro | Arg | Ala | Phe | His | Leu |  |
| 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |  |
| Ala | Cys | Leu | Ser | Pro | Pro | Leu | Arg | Glu | Ile | Pro | Ser | Gly | Thr | Trp | Arg |  |
| 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |     |     |     |     |  |
| Cys | Ser | Ser | Cys | Leu | Gln | Ala | Thr | Val | Gln | Glu | Val | Gln | Pro | Arg | Ala |  |
| 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |     |     |     |  |
| Glu | Glu | Pro | Arg | Pro | Gln | Glu | Pro | Pro | Val | Glu | Thr | Pro | Leu | Pro | Pro |  |
| 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |     |     |  |
| Gly | Leu | Arg | Ser | Ala | Gly | Glu | Glu | Val | Arg | Gly | Pro | Pro | Gly | Glu | Pro |  |
| 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |     |  |
| Leu | Ala | Gly | Met | Asp | Thr | Thr | Leu | Val | Tyr | Lys | His | Leu | Pro | Ala | Pro |  |
| 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |  |
| Pro | Ser | Ala | Ala | Pro | Leu | Pro | Gly | Leu | Asp | Ser | Ser | Ala | Leu | His | Pro |  |
| 405 |     |     |     |     | 410 |     |     |     |     | 415 |     |     |     |     |     |  |
| Leu | Leu | Cys | Val | Ala | Pro | Glu | Gly | Gln | Gln | Asn | Leu | Ala | Pro | Gly | Ala |  |
| 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |     |     |     |  |
| Arg | Cys | Gly | Val | Cys | Gly | Asp | Gly | Thr | Asp | Val | Leu | Arg | Cys | Thr | His |  |
| 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |     |     |  |
| Cys | Ala | Ala | Ala | Phe | His | Trp | Arg | Cys | His | Phe | Pro | Ala | Gly | Thr | Ser |  |

|   |     |         |
|---|-----|---------|
| 450   | 455 | 460     |
| Arg Pro Gly Thr Gly Leu Arg Cys Arg Ser Cys Ser Gly Asp Val Thr |     |         |
| 465   | 470 | 475 480 |
| Pro Ala Pro Val Glu Gly Val Leu Ala Pro Ser Pro Ala Arg Leu Ala |     |         |
|   | 485 | 490 495 |
| Pro Gly Pro Ala Lys Asp Asp Thr Ala Ser His Glu Pro Ala Leu His |     |         |
|   | 500 | 505 510 |
| Arg Asp Asp Leu Glu Ser Leu Leu Ser Glu His Thr Phe Asp Gly Ile |     |         |
|   | 515 | 520 525 |
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| Ser   |     |         |
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|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Trp | Leu | Val | Tyr | Ser | Ser | Gly | Ala | Pro | Gly | Thr | Gln | Gln | Pro | Ala | Arg |     |  |
|     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |     |     |  |
| aac | cgg | gtt | ttc | ttc | cca | ata | ggg | atg | gcc | ccg | ggg | ggg | gtc | tgt | tcg | 335 |  |
| Asn | Arg | Val | Phe | Phe | Pro | Ile | Gly | Met | Ala | Pro | Gly | Gly | Val | Cys | Ser |     |  |
|     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |     |     |  |
| aga | cca | gat | gga | tgg | gga | aca | ggg | ggg | cag | ggc | aga | att | tca | ggc | cct | 383 |  |
| Arg | Pro | Asp | Gly | Trp | Gly | Thr | Gly | Gly | Gln | Gly | Arg | Ile | Ser | Gly | Pro |     |  |
|     |     | 35  |     |     |     | 40  |     |     |     |     | 45  |     |     |     |     |     |  |
| ggc | agc | atg | gga | gca | ggg | cag | aga | ctg | ggg | agt | tca | ggg | acc | cag | aga | 431 |  |
| Gly | Ser | Met | Gly | Ala | Gly | Gln | Arg | Leu | Gly | Ser | Ser | Gly | Thr | Gln | Arg |     |  |
|     | 50  |     |     |     | 55  |     |     |     | 60  |     |     |     |     |     | 65  |     |  |
| tgc | tgc | tgg | ggg | agc | tgt | ttt | ggg | aag | gag | gtg | gct | ctc | agg | agg | gtg | 479 |  |
| Cys | Cys | Trp | Gly | Ser | Cys | Phe | Gly | Lys | Glu | Val | Ala | Leu | Arg | Arg | Val |     |  |
|     |     |     |     | 70  |     |     |     | 75  |     |     |     |     | 80  |     |     |     |  |
| ctg | cac | ccc | agc | cca | gtc | tgc | atg | ggc | gtc | tct | tgc | ctg | tgc | cag | aag | 527 |  |
| Leu | His | Pro | Ser | Pro | Val | Cys | Met | Gly | Val | Ser | Cys | Leu | Cys | Gln | Lys |     |  |
|     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |     |     |  |
| aat | gag | gac | gag | tgt | gcc | gtg | tgt | cgg | gac | ggc | ggg | gag | ctc | atc | tgc | 575 |  |
| Asn | Glu | Asp | Glu | Cys | Ala | Val | Cys | Arg | Asp | Gly | Gly | Glu | Leu | Ile | Cys |     |  |
|     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |     |  |
| tgt | gac | ggc | tgc | cct | cgg | gcc | ttc | cac | ctg | gcc | tgc | ctg | tcc | cct | ccg | 623 |  |
| Cys | Asp | Gly | Cys | Pro | Arg | Ala | Phe | His | Leu | Ala | Cys | Leu | Ser | Pro | Pro |     |  |
|     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |     |     |  |
| ctc | cgg | gag | atc | ccc | agt | ggg | acc | tgg | agg | tgc | tcc | agc | tgc | ctg | cag | 671 |  |
| Leu | Arg | Glu | Ile | Pro | Ser | Gly | Thr | Trp | Arg | Cys | Ser | Ser | Cys | Leu | Gln |     |  |
|     | 130 |     |     |     | 135 |     |     |     | 140 |     |     |     | 145 |     |     |     |  |
| gca | aca | gtc | cag | gag | gtg | cag | ccc | cgg | gca | gag | gag | ccc | cgg | ccc | cag | 719 |  |
| Ala | Thr | Val | Gln | Glu | Val | Gln | Pro | Arg | Ala | Glu | Glu | Pro | Arg | Pro | Gln |     |  |
|     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |     |     |     |  |
| gag | cca | ccc | gtg | gag | acc | ccg | ctc | ccc | ccg | ggg | ctt | agg | tcg | gcg | gga | 767 |  |
| Glu | Pro | Pro | Val | Glu | Thr | Pro | Leu | Pro | Pro | Gly | Leu | Arg | Ser | Ala | Gly |     |  |
|     |     |     | 165 |     |     |     | 170 |     |     |     |     | 175 |     |     |     |     |  |
| gag | gag | gta | aga | ggg | cca | cct | ggg | gaa | ccc | cta | gcc | ggc | atg | gac | acg | 815 |  |
| Glu | Glu | Val | Arg | Gly | Pro | Pro | Gly | Glu | Pro | Leu | Ala | Gly | Met | Asp | Thr |     |  |
|     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |     |     |  |
| act | ctt | gtc | tac | aag | cac | ctg | ccg | gct | ccg | cct | tct | gca | gcc | ccg | ctg | 863 |  |

|   |      |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
|---|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|
| Thr   | Leu  | Val | Tyr | Lys | His | Leu | Pro | Ala | Pro | Pro | Ser | Ala | Ala | Pro | Leu |  |  |
| 195   |      |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     |  |  |
| cca ggt ctg gac tcc tcg gcc ctg cac ccc cta ctg tgt gtg ggt cct   | 911  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| Pro Gly Leu Asp Ser Ser Ala Leu His Pro Leu Leu Cys Val Gly Pro   |      |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| 210   | 215  | 220 | 225 |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| gag ggt cag cag aac ctg gct cct ggt gcg cgt tgc ggg gtg tgc gga   | 959  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| Glu Gly Gln Gln Asn Leu Ala Pro Gly Ala Arg Cys Gly Val Cys Gly   |      |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| 230   | 235  | 240 |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| gat ggt acg gac gtg ctg cgg tgt act cac tgc gcc gct gcc ttc cac   | 1007 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| Asp Gly Thr Asp Val Leu Arg Cys Thr His Cys Ala Ala Ala Phe His   |      |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| 245   | 250  | 255 |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| tgg cgc tgc cac ttc cca gcc ggc acc tcc cgg ccc ggg acg ggc ctg   | 1055 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| Trp Arg Cys His Phe Pro Ala Gly Thr Ser Arg Pro Gly Thr Gly Leu   |      |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| 260   | 265  | 270 |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| cgc tgc aga tcc tgc tca gga gac gtg acc cca gcc cct gtg gag ggg   | 1103 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| Arg Cys Arg Ser Cys Ser Gly Asp Val Thr Pro Ala Pro Val Glu Gly   |      |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| 275   | 280  | 285 |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| gtg ctg gcc ccc agc ccc gcc cgc ctg gcc cct ggg cct gcc aag gat   | 1151 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| Val Leu Ala Pro Ser Pro Ala Arg Leu Ala Pro Gly Pro Ala Lys Asp   |      |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| 290   | 295  | 300 | 305 |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| gac act gcc agt cac gag ccc gct ctg cac agg gat gac ctg gag tcc   | 1199 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| Asp Thr Ala Ser His Glu Pro Ala Leu His Arg Asp Asp Leu Glu Ser   |      |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| 310   | 315  | 320 |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| ctt ctg agc gag cac acc ttc gat ggc atc ctg cag tgg gcc atc cag   | 1247 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| Leu Leu Ser Glu His Thr Phe Asp Gly Ile Leu Gln Trp Ala Ile Gln   |      |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| 325   | 330  | 335 |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| agc atg gcc cgt ccg gcg gcc ccc ttc ccc tcc tga cccagatgg         | 1293 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| Ser Met Ala Arg Pro Ala Ala Pro Phe Pro Ser                       |      |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| 340   | 345  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| ccgggacatg cagctctgat gagagagtgc tgagaaggac acctccttcc tcagtcctgg | 1353 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| aagccggccg gctgggatca agaaggggac agcgccacct cttgtcagtg ctcggctgta | 1413 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| aacagctctg tgtttctggg gacaccagcc atcatgtgcc tggaaattaa accctgcccc | 1473 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| acttctctac tctggaagtc cccgggagcc tctccttgcc tggtgaccta ctaaaaatat | 1533 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
| aaaaattagc tg   | 1545 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |

<210> 4

<211> 348

<212> PRT

<213> Homo sapiens

<400> 4

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1 5 10 15

Arg Asn Arg Val Phe Phe Pro Ile Gly Met Ala Pro Gly Gly Val Cys  
20 25 30

Ser Arg Pro Asp Gly Trp Gly Thr Gly Gly Gln Gly Arg Ile Ser Gly  
35 40 45

Pro Gly Ser Met Gly Ala Gly Gln Arg Leu Gly Ser Ser Gly Thr Gln  
50 55 60

Arg Cys Cys Trp Gly Ser Cys Phe Gly Lys Glu Val Ala Leu Arg Arg  
65 70 75 80

Val Leu His Pro Ser Pro Val Cys Met Gly Val Ser Cys Leu Cys Gln  
85 90 95

Lys Asn Glu Asp Glu Cys Ala Val Cys Arg Asp Gly Gly Glu Leu Ile  
100 105 110

Cys Cys Asp Gly Cys Pro Arg Ala Phe His Leu Ala Cys Leu Ser Pro  
115 120 125

Pro Leu Arg Glu Ile Pro Ser Gly Thr Trp Arg Cys Ser Ser Cys Leu  
130 135 140

Gln Ala Thr Val Gln Glu Val Gln Pro Arg Ala Glu Glu Pro Arg Pro  
145 150 155 160

Gln Glu Pro Pro Val Glu Thr Pro Leu Pro Pro Gly Leu Arg Ser Ala  
165 170 175

Gly Glu Glu Val Arg Gly Pro Pro Gly Glu Pro Leu Ala Gly Met Asp  
180 185 190

Thr Thr Leu Val Tyr Lys His Leu Pro Ala Pro Pro Ser Ala Ala Pro  
195 200 205

Leu Pro Gly Leu Asp Ser Ser Ala Leu His Pro Leu Leu Cys Val Gly



|   |     |         |
|---|-----|---------|
| 210   | 215 | 220     |
| Pro Glu Gly Gln Gln Asn Leu Ala Pro Gly Ala Arg Cys Gly Val Cys |     |         |
| 225   | 230 | 235 240 |
| Gly Asp Gly Thr Asp Val Leu Arg Cys Thr His Cys Ala Ala Ala Phe |     |         |
|   | 245 | 250 255 |
| His Trp Arg Cys His Phe Pro Ala Gly Thr Ser Arg Pro Gly Thr Gly |     |         |
|   | 260 | 265 270 |
| Leu Arg Cys Arg Ser Cys Ser Gly Asp Val Thr Pro Ala Pro Val Glu |     |         |
|   | 275 | 280 285 |
| Gly Val Leu Ala Pro Ser Pro Ala Arg Leu Ala Pro Gly Pro Ala Lys |     |         |
|   | 290 | 295 300 |
| Asp Asp Thr Ala Ser His Glu Pro Ala Leu His Arg Asp Asp Leu Glu |     |         |
| 305   | 310 | 315 320 |
| Ser Leu Leu Ser Glu His Thr Phe Asp Gly Ile Leu Gln Trp Ala Ile |     |         |
|   | 325 | 330 335 |
| Gln Ser Met Ala Arg Pro Ala Ala Pro Phe Pro Ser                 |     |         |
|   | 340 | 345     |

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 ctgctctcag ctggggcccg ggggtgggccc ggcgcccctg ctatagccag gaggtcaagg 120  
 atccactggg aatgccatgc tcattcttcg tccccagcat ggtttcttaa tggggtagaa 180

gcaggtcggg agagacctcc ctgggcctgg ccccactgcc ctgtgaggaa gggttc atg 239  
Met  
1

tgg ttg gtg tac agt tcc ggg gcc cct gga acg cag cag cct gca aga 287  
Trp Leu Val Tyr Ser Ser Gly Ala Pro Gly Thr Gln Gln Pro Ala Arg  
5 10 15

aac cgg gtt ttc ttc cca ata ggg atg gcc ccg ggg ggt gtc tgt tgg 335  
Asn Arg Val Phe Phe Pro Ile Gly Met Ala Pro Gly Gly Val Cys Trp  
20 25 30

aga cca gat gga tgg gga aca ggt ggt cag ggc aga att tca ggc cct 383  
Arg Pro Asp Gly Trp Gly Thr Gly Gly Gln Gly Arg Ile Ser Gly Pro  
35 40 45

ggc agc atg gga gca ggg cag aga ctg ggg agt tca ggt acc cag aga 431  
Gly Ser Met Gly Ala Gly Gln Arg Leu Gly Ser Ser Gly Thr Gln Arg  
50 55 60 65

tgc tgc tgg ggg agc tgt ttt ggg aag gag gtg gct ctc agg agg gtg 479  
Cys Cys Trp Gly Ser Cys Phe Gly Lys Glu Val Ala Leu Arg Arg Val  
70 75 80

ctg cac ccc agc cca gtc tgc atg ggc gtc tct tgc ctg tgc cag aag 527  
Leu His Pro Ser Pro Val Cys Met Gly Val Ser Cys Leu Cys Gln Lys  
85 90 95

aat gag gac gag tgt gcc gtg tgt cgg gac ggc ggg gag ctc atc tgc 575  
Asn Glu Asp Glu Cys Ala Val Cys Arg Asp Gly Gly Glu Leu Ile Cys  
100 105 110

tgt gac ggc tgc cct cgg gcc ttc cac ctg gcc tgc ctg tcc cct ccg 623  
Cys Asp Gly Cys Pro Arg Ala Phe His Leu Ala Cys Leu Ser Pro Pro  
115 120 125

ctc cgg gag atc ccc agt ggg acc tgg agg tgc tcc agc tgc ctg cag 671  
Leu Arg Glu Ile Pro Ser Gly Thr Trp Arg Cys Ser Ser Cys Leu Gln  
130 135 140 145

gca aca gtc cag gag gtg cag ccc cgg gca gag gag ccc cgg ccc cag 719  
Ala Thr Val Gln Glu Val Gln Pro Arg Ala Glu Glu Pro Arg Pro Gln  
150 155 160

gag cca ccc gtg gag acc ccg ctc ccc ccg ggg ctt agg tcg gcg gga 767  
Glu Pro Pro Val Glu Thr Pro Leu Pro Pro Gly Leu Arg Ser Ala Gly  
165 170 175

gag gag ccc cgc tgc cag ggc tgg act cct cgg ccc tgc acc ccc tac 815  
 Glu Glu Pro Arg Cys Gln Gly Trp Thr Pro Arg Pro Cys Thr Pro Tyr  
           180                                  185                                  190

tgt gtg tgg gtc ctg agg gtc agc aga acc tgg ctc ctg gtg cgc gtt 863  
 Cys Val Trp Val Leu Arg Val Ser Arg Thr Trp Leu Leu Val Arg Val  
           195                                  200                                  205

gcg ggg tgt gcg gag atg gta cgg acg tgc tgc ggt gta ctc act gcg 911  
 Ala Gly Cys Ala Glu Met Val Arg Thr Cys Cys Gly Val Leu Thr Ala  
 210                                  215                                  220                                  225

ccg ctg cct tcc act ggc gct gcc act tcc cag ccg gca cct ccc ggc 959  
 Pro Leu Pro Ser Thr Gly Ala Ala Thr Ser Gln Pro Ala Pro Pro Gly  
                                   230                                  235                                  240

ccg gga cgg gcc tgc gct gca gat cct gct cag gag acg tga 1001  
 Pro Gly Arg Ala Cys Ala Ala Asp Pro Ala Gln Glu Thr  
                                   245                                  250                                  255

ccccagcccc tgtggagggg gtgctggccc ccagccccgc ccgcctggcc cctgggcctg 1061

ccaaggatga cactgccagt cacgagcccg ctctgcacag ggatgacctg gagtcccttc 1121

tgagcgagca caccttcgat ggcatcctgc agtggggccat ccagagcatg gcccgctccg 1181

cggccccctt cccctcctga cccagatgg ccgggacatg cagctctgat gagagagtgc 1241

tgagaaggac acctccttcc tcagtcctgg aagccggccg gctgggatca agaaggggac 1301

agcgccacct cttgtcagtg ctcggtgta aacagctctg tgtttctggg gacaccagcc 1361

atcatgtgcc tggaaattaa accctgcccc acttctctac tctggaagtc cccgggagcc 1421

tctccttgcc tggtgacctg ctaaaaatat aaaaattagc tg 1463

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<211> 254

<212> PRT

<213> Homo sapiens

<400> 6

Met Trp Leu Val Tyr Ser Ser Gly Ala Pro Gly Thr Gln Gln Pro Ala  
   1                                  5                                  10                                  15

Arg Asn Arg Val Phe Phe Pro Ile Gly Met Ala Pro Gly Gly Val Cys

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|
|     | 20  |     | 25  |     | 30  |     |     |     |     |     |     |     |     |     |     |  |  |
| Trp | Arg | Pro | Asp | Gly | Trp | Gly | Thr | Gly | Gly | Gln | Gly | Arg | Ile | Ser | Gly |  |  |
|     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |     |  |  |
| Pro | Gly | Ser | Met | Gly | Ala | Gly | Gln | Arg | Leu | Gly | Ser | Ser | Gly | Thr | Gln |  |  |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |  |  |
| Arg | Cys | Cys | Trp | Gly | Ser | Cys | Phe | Gly | Lys | Glu | Val | Ala | Leu | Arg | Arg |  |  |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |  |  |
| Val | Leu | His | Pro | Ser | Pro | Val | Cys | Met | Gly | Val | Ser | Cys | Leu | Cys | Gln |  |  |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |  |  |
| Lys | Asn | Glu | Asp | Glu | Cys | Ala | Val | Cys | Arg | Asp | Gly | Gly | Glu | Leu | Ile |  |  |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |  |  |
| Cys | Cys | Asp | Gly | Cys | Pro | Arg | Ala | Phe | His | Leu | Ala | Cys | Leu | Ser | Pro |  |  |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |  |  |
| Pro | Leu | Arg | Glu | Ile | Pro | Ser | Gly | Thr | Trp | Arg | Cys | Ser | Ser | Cys | Leu |  |  |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |  |  |
| Gln | Ala | Thr | Val | Gln | Glu | Val | Gln | Pro | Arg | Ala | Glu | Glu | Pro | Arg | Pro |  |  |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |  |  |
| Gln | Glu | Pro | Pro | Val | Glu | Thr | Pro | Leu | Pro | Pro | Gly | Leu | Arg | Ser | Ala |  |  |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |  |  |
| Gly | Glu | Glu | Pro | Arg | Cys | Gln | Gly | Trp | Thr | Pro | Arg | Pro | Cys | Thr | Pro |  |  |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |  |  |
| Tyr | Cys | Val | Trp | Val | Leu | Arg | Val | Ser | Arg | Thr | Trp | Leu | Leu | Val | Arg |  |  |
|     | 195 |     |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |  |  |
| Val | Ala | Gly | Cys | Ala | Glu | Met | Val | Arg | Thr | Cys | Cys | Gly | Val | Leu | Thr |  |  |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |  |  |
| Ala | Pro | Leu | Pro | Ser | Thr | Gly | Ala | Ala | Thr | Ser | Gln | Pro | Ala | Pro | Pro |  |  |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     | 240 |     |  |  |
| Gly | Pro | Gly | Arg | Ala | Cys | Ala | Ala | Asp | Pro | Ala | Gln | Glu | Thr |     |     |  |  |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     |     |     |  |  |

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<220>

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20

<210> 8

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<223> Description of Artificial Sequence: PRIMER

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22

<210> 9

<211> 20

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: PRIMER

<400> 9

aggggacagg caggccaggt

20

<210> 10

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PRIMER

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24

<210> 11

<211> 20

<212> DNA

<213> Artificial Sequence

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<210> 12

<211> 23

<212> DNA

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ggattcagac catgtcagct tca

23

<210> 13

<211> 21

<212> DNA

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<400> 13

gtgctgttca aggatcacao c

21

<210> 14

<211> 21

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: PRIMER

<400> 14

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21

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 <400> 17  
 agaaaaagagctgtaccctgtg 22  
  
 <210> 18  
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21

<210> 20

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<400> 20

acgggctcct caaacaccac t

21

<210> 21

<211> 24

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: PRIMER

<400> 21

tggagatggg caggccgcag ggtg

24

<210> 22

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PRIMER

<400> 22

cagtccagct gggctgagca ggtg

24

<210> 23

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<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PRIMER

<400> 23

gcggctccaa gaagtgcata cagg

24

<210> 24

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PRIMER

<400> 24

ctccaccctg caaggaagag gggc

24

<210> 25

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PRIMER

<400> 25

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Thr | Leu | His | Leu | Lys | Glu | Lys | Glu | Gly | Cys | Pro | Val | Gln | Ala | Phe | His |
| 1   |     |     |     | 5   |     |     |     | 10  |     |     |     |     |     | 15  |     |

<210> 26

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PRIMER

<400> 26

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cys | Lys | Asn | Lys | Ala | Arg | Ser | Ser | Ser | Gly | Pro | Lys | Pro | Leu | Val |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |

<210> 27

<211> 24  
<212> DNA  
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<220>  
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<400> 27  
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<210> 28  
<211> 24  
<212> DNA  
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<220>  
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<400> 28  
cctggatgta cttcttgag ccgc 24

<210> 29  
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<400> 29  
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<210> 30  
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<400> 30  
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<210> 31

<211> 24  
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 <210> 32  
 <211> 24  
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 <400> 32  
 caccaggcaa ggagaggctc ccgg 24  
  
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 <400> 33  
 ccaccccatg gcgacggacg 20  
  
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 ggaattcgga ggggaagggg gccgccgga 29  
  
 <210> 35

<211> 24  
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ggactgagga aggaggtgtc cttc

24

<210> 36

<211> 20

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: PRIMER

<400> 36

Asp Gly Ile Leu Gln Trp Ala Ile Gln Ser Met Ala Arg Pro Ala Ala  
1 5 10 15

Pro Phe Pro Ser  
20